

Applicants: Nicole Suciu-Foca, et al.
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REMARKS

Claims 1-57 are pending in the subject application. Claims 1-33, 37 and 39-57 have been withdrawn by the Examiner. No claims have been added or canceled by this Amendment. Applicants have amended the specification to update the priority paragraph, correct certain typographic errors and to insert SEQ. ID. NOs: where required. Applicants have also amended claim 34 to correct a typographic error. Applicants have further amended claims 35, 36 and 38 to correctly refer to independent claim number 34 upon which they depend, which was previously referred to as claim 33 due to the miscounting of claim 19 as claim 18. Applicants maintain that these amendments raise no issue of new matter. Accordingly, upon entry of this Amendment, claims 34-36 and 38 will be pending and under examination.

Formalities

Amendment to Priority Paragraph

The Examiner requested that the priority paragraph one page 1, line 6 be updated to reflect the status of parent U.S. Application No. 09/333,809.

In response, applicants have amended the priority paragraph to reflect the status of U.S. Application No. 09/333,809, now U.S. Patent No. 6,667,175, issued December 23, 2003.

Sequence Listing

The Examiner stated that the subject application fails to comply with the requirements of 37 C.F.R. §1.821-1.825.

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The Examiner stated that applicants must provide (a) an initial computer readable form (CRF) of the sequence listing, (b) an initial paper copy of the sequence listing and an amendment directing its entry into the application, and (c) a statement that the content of the sequence information recorded in computer readable form is identical to that of the paper sequence listing and, where applicable, includes no new matter, as required by 37 C.F.R. 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d).

In response, applicants submit (a) a paper copy of the Sequence Listing attached hereto as **Exhibit A**, (b) a Request to use the CRF of the sequence listing from U.S. Serial No. 09/333,809, now U.S. Patent No. 6,667,175, attached hereto as **Exhibit B**, and (c) a statement in accordance with 37 C.F.R. §1.821(f) attached hereto as **Exhibit C**, certifying that (i) the CRF and written sequence listing contain the same sequence information, and (ii) the sequence listing contains no new matter.

Title of Application

The Examiner also stated that the title of the invention is not descriptive, and that a new title is required that is indicative of the invention to which the claims are directed.

In response, applicants have amended the title such that it is indicative of the invention to which claims 34-36 and 38 are directed.

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Information Disclosure Statement

The Examiner stated that the references submitted with the Information Disclosure Statement in connection with parent U.S. Patent Application No. 09/333,809 cannot be found and request that such references be resubmitted.

In response, applicants enclose as **Exhibit D** a copy of the Information Disclosure Statement filed on August 9, 1999 in connection with parent U.S. Patent Application No. 09/333,809.

Typographic Errors

The Examiner also points out the presence of minor typographic errors and requests the correction thereof.

In response, applicants have amended the specification to correct the specific examples pointed out by the Examiner, and will review the rest of the specification and correct any additional typographic errors in a future Amendment.

Objection to Claims 34 and 35

The Examiner objected to claim 34 because the word "tyrosine" is misspelled therein.

In response, applicants have amended claim 34 to correct the misspelling of "tyrosine".

The Examiner also objected to claim 35, which contains an extra comma following the word "(MIR7)".

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In response, applicants have amended claim 35 to delete the extra comma.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 34, 36 and 38 under 35 U.S.C. §112, first paragraph as allegedly lacking enablement.

Specifically, the Examiner alleges that although the specification is enabling for a method of inducing anergic T helper cells which comprise overexpressing in the APC mRNA which encodes at least one monocyte inhibitory receptor (MIR), wherein said MIR is selected from the group consisting of ILT4, ILT2 and ILT3, it does not reasonably provide enablement for a method of inducing T helper cells which comprise overexpressing in the APC mRNA which encodes at least any one of MIR. Accordingly, the Examiner alleges that one skilled in the art could not practice the claimed invention without undue experimentation.

In response, applicants respectfully traverse.

Claim 34, and dependent claims 35, 36 and 38, provide a method of inducing anergic T helper cells. This method comprises (a) incubating antigen presenting cells (APC) with allospecific T suppressor cells (Ts), (b) overexpressing in the APC mRNA which encodes at least one monocyte inhibitory receptor (MIR), in a mixture of cells comprising the APCs from step (a), wherein overexpression of MIR transmits negative inhibitory signals to recruit an inhibitory signaling molecule, tyrosine phosphatase SHP-1 such that the APC are rendered tolerogenic and (c) incubating the APCs from step (b) with T helper cells (Th) to induce Th anergy.

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For a claim to be enabled, it is necessary that one skilled in the art at the time of filing could practice the claimed invention in view of the specification without undue experimentation. In the event some experimentation were required to practice the invention, which applicants do not concede, the need for such experimentation does not by itself constitute a lack of enablement. Rather, for that to happen, the experimentation must be undue.

Here, applicants have provided a representative number of members of the Monocyte Inhibitory Receptors (MIR), i.e. MIR-10 or ILT4, MIR7 or ILT2 and ILT3, to enable the pending claims. Applicants have also described the MIR10, MIR7 and ILT3 as belonging to a family of leukocyte inhibitory receptors (LIRs) which bear homology to killer inhibitory receptors (see page 118, lines 18-20). Applicants have also described the interaction of MIR molecules with MHC-class I molecules via Ig-like domains, and the recruitment of an inhibitory signaling molecule, tyrosine phosphatase SHP-1 (see page 118, lines 21-24).

The Examiner cites Papanikolaou, et al. and Chang, et al. to support the rejection of claims 34, 36 and 38 under 3 U.S.C. §112, first paragraph.

Specifically, the Examiner alleges that Papanikolaou, et al. teaches that there are differences in binding affinity among MIRs to their receptors, and that these differences would result in variation in the strength of tolerizing signals that are generated by said MIRs in APC.

In response, applicants maintain that the Examiner has erroneously expanded the teachings of Papanikolaou, et al.

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As the Examiner has stated himself, Papanikolaou, et al. teaches that there are differences in binding affinity among MIRs to their receptors, and that these differences would result in variation in the strength of tolerizing signals that are generated by said MIRs in APCs. Applicants maintain that nowhere in the cited article does it teach that certain MIRs will generate *no* tolerizing signal, only that there may be *variations* in the *strength* of the tolerizing signal among MIRs. The Examiner has not cited any evidence supporting his position that overexpression of any MIR will not provide *any* negative inhibitory signal.

The Examiner further cites Chang, et al., which allegedly teaches that *only* the upregulation of specific MIRs, i.e., ILT3 and ILT4, have an immunoregulatory effect upon APCs.

In response, applicants maintain that the Examiner has also erroneously expanded the teachings of Chang, et al. Applicants maintain that nowhere does Chang, et al. teach that ILT-3 and ILT-4 are the *only* MIRs capable of generating a negative inhibitory signal. In fact, the Examiner himself concedes that the method recited in claim 34 is enabled wherein the MIR is ILT-2.

Accordingly, applicants maintain that claims 34, 36 and 38 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Objection to Claim 35

The Examiner objected to claim 35 as dependent upon a rejected claim. In response, applicants maintain that the rejected claim upon which it depends is in condition for allowance, and that the Examiner's objection should be

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withdrawn.

Summary

In view of the above remarks, applicants maintain that the pending claims are in condition for allowance, and respectfully request allowance.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

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